

National Aeronautics and Space Administration Johnson Space Center Human Exploration and Operations Mission Directorate Human Research Program Houston, TX 77058

Human Exploration Research Opportunities (HERO)

NNJ15ZSA001N-NSBRI Appendix B

The National Space Biomedical Research Institute (NSBRI)



Research and Technology Development to Support Crew Health and Performance in Space Exploration Missions

Step-1 Proposals Due: September 4, 2015, 5 PM Eastern Time Notification of Proposal Status: September 24, 2015

Step-2 Proposals (By Invitation) Due: November 23, 2015, 5 PM Eastern Time You must read and understand this solicitation in its entirety to prepare a competitive proposal. Key requirements are identified here:

- The information and specific submission instructions in this NRA supersede that found in the NASA Guidebook for Proposers. Proposals that do not conform to the requirements in this NRA may be declared noncompliant and declined without review (sections D.4 and E.3.a).
- For Step-1 and Step-2 proposals: You and your organization must be registered with NSPIRES. Your proposal must be submitted by an authorized representative of your organization. All team members listed on the proposal must be registered with NSPIRES.
- For Step-1 and invited Step-2 proposals: Your specific aims must address the research emphases in this solicitation, and must be clearly outlined in the project description of your proposal.
- For Step-2 proposals: Proposals must identify Integrated Research Plan (IRP) risks and gaps addressed by the research.
- For Step-2 proposals: The length of the project description of the proposal cannot exceed 20 pages using standard (12 point) type.
- For Step-2 proposals: Investigators submitting a proposal in response to this solicitation, and whose most recent submission that included similar specific aims to any NASA or NSBRI sponsored research announcement was not accepted, must address prior review comments (2 pages maximum).
- Investigators resubmitting a proposal in response to this solicitation may only submit a proposal with similar hypothesis(es) and aims a total of three times (original submission plus two resubmissions). Significant changes must be made to the proposal hypothesis(es) and specific aims for consideration after the third attempt or the proposal will be declined without further review.
- For Step-2 proposals: If you have received past NASA or NSBRI supported research within the last three years, you must provide specifics (2 pages maximum) of the productivity of your research in a section separate from the project description.
- For Step-2 proposals: If using vertebrate animals, your proposal must meet requirements of the Vertebrate Animal Scientific Review section of this solicitation.
- For Step-2 proposals: Your proposal must meet requirements of the Compliance Review section of this solicitation.
- For Step-2 proposals: If applicable, the Analog Study Resource Worksheet should be included.
- NASA HRP has adopted the NIH policy concerning the sharing of software produced through grants.
- Step-1 and Step-2 selection decision information can be accessed after the selection announcement date listed in this solicitation. After logging in, the PI selects the "Proposals" link, the "Submitted Proposals/NOIs" link, and then clicks on the proposal submitted to the solicitation identified above. The document(s) provided by NASA will be displayed under the heading "PI Information Package" located at the bottom of the "View Proposal" page.

Appendix B

NSBRI Research and Technology Development to Support Crew Health and Performance in Space Exploration Missions

A. Funding Opportunity Description

1. Introduction

The National Space Biomedical Research Institute (NSBRI) is a non-profit organization competitively-selected by NASA that uses an integrated team approach to advance biomedical research and countermeasure development. NSBRI works in partnership with NASA. Research, development, testing and evaluation are conducted with the goal of ensuring safe and productive long-term human exploration of space. Proposals that lead to the development of operationally relevant countermeasures in high priority areas are encouraged. Moreover, where appropriate, applications should take into consideration research resources, as listed in section G of the HERO Overview. The HERO Overview document is posted alongside this solicitation at http://nspires.nasaprs.com. The current NSBRI research program consists of approximately 60 science and technology projects organized into research teams.

This section of the NASA Research Announcement (NRA), Appendix B, solicits proposals for the opportunity to become a **member of an integrated Science and Technology team** of NSBRI.

Research Emphases:

The NSBRI portion of this NRA solicits proposals addressing research emphases in one of the following Science and Technology discipline Teams:

- 1) Human Factors and Performance
- 2) Musculoskeletal Alterations
- 3) Neurobehavioral and Psychosocial Factors
- 4) Radiation Effects
- 5) Smart Medical Systems and Technology

Proposals on additional topics not specifically mentioned herein, but relevant to Human Research Program (HRP) Risks and Gaps, may be submitted to the NASA HRP Omnibus Opportunity section of the NRA posted alongside this solicitation at <u>http://nspires.nasaprs.com</u>. These may include topics that would be included in any of the seven NSBRI Science and Technology discipline Teams.

Proposals solicited through this NRA will use a two-step proposal process. Only proposers submitting Step-1 proposals determined to be relevant with respect to the Research

Emphases outlined in Section A.2 of this appendix will be invited to submit full Step-2 proposals.

Proposals that impact more than one emphasis should be directed to one primary research area, although a secondary research area may be designated if the proposal has substantial overlap with that area. Studies using integrated methods are encouraged. Proposals that synergistically bridge multiple disciplines for the purpose of modeling the effects of microgravity on the human body to aid in the development and testing of countermeasures, or proposals to develop technologies that enable research in one or more NSBRI research area(s) are strongly encouraged.

It is critical for investigators to read all of the instructions in this NRA carefully. All proposals will undergo peer review using the same processes and procedures. All proposals must be submitted electronically, and all proposers are required to use NASA Solicitation and Proposal Integrated Review and Evaluation System (NSPIRES). Any proposals not submitted through the NSPIRES portal and sent directly to NSBRI by email, fax or other means will be returned without review. Programmatic balance is maintained by the selection official for the research program.

Information describing the research needs for human space exploration as defined by NASA's HRP can be found in Section B of the HERO Overview. Proposals to NSBRI must address the research emphases outlined by Science & Technology team in Section A.2 of this document.

Investigators are encouraged to review summaries of currently funded research by accessing NSBRI's website at <u>http://www.nsbri.org</u> and the NASA Space Life & Physical Sciences Research & Applications Division Task Book at: <u>http://taskbook.nasaprs.com/peer_review/index.cfm</u>.

NSBRI is governed by a consortium of twelve institutions: Baylor College of Medicine, Brookhaven National Laboratory, Harvard Medical School, The Johns Hopkins University, Massachusetts Institute of Technology, Morehouse School of Medicine, Mount Sinai School of Medicine, Rice University, Texas A&M University, the University of Arkansas for Medical Sciences, the University of Pennsylvania Health System, and the University of Washington. The Institute's Headquarters are located in Houston at Baylor College of Medicine.

Consortium membership is not a requirement for research program participation.

NSBRI's External Advisory Council (EAC) is responsible for advising Institute management concerning program strategy, as well as tactical implementation and effectiveness. NSBRI also includes a User Panel of former and current astronauts and flight surgeons, which is responsible for assuring that the research program is focused squarely on astronaut health, safety and performance. The User Panel advises senior management on the operational relevance and feasibility of science and technology projects. An Industry Forum of representatives from space and biomedical companies advises and assists NSBRI concerning Earth-based applications of Institute research. The Institute coordinates its research activities with NASA through several committees and working groups, including a joint NASA/NSBRI Steering Committee. In addition to its research program, NSBRI has developed a robust Career Development and

Outreach Program that leverages the Institute's core research activities.

2. Research Teams and Emphases

Each of the NSBRI science and technology teams consists of a set of complementary projects focused in a particular discipline. Team Leaders oversee the value added among the projects, to ensure that the integrated team approach leads to more effective outcome-driven research than might be attainable by a single project alone. Proposers are encouraged to look at each of the seven Team Executive Summaries and the current composition of the teams in preparing their proposals. Proposers are also required to: (1) Define clear milestones for their project; and (2) If appropriate, describe a plan as to how they intend to collaborate with any NASA or NSBRI scientists, engineers, flight surgeons, and astronauts. An explanation should be provided as to how any collaboration will: (1) Increase the likelihood of success; (2) Improve the delivery of results or products; and (3) Positively impact the proposed research.

Proposers applying to NSBRI's integrated research program must identify the primary NSBRI discipline team and the secondary discipline NSBRI team (if applicable) responsible for the area their proposal is addressing below. Proposers must also identify the countermeasure readiness level (CRL) and/or technology readiness level (TRL) of their research proposal. Proposers should refer to Figures 1 and 2 in the Overview for detailed descriptions of the CRL and TRL scales. This information will be collected online as Cover Page elements during electronic proposal submission. Research emphases may relate to one or more type of proposal (ground-based or analog definition), as described in section E of the HERO Overview.

Proposals must be responsive to the research emphases specifically described in the bullet points below in order to be reviewed as significant to the goals of this solicitation. The proposed research approach must adhere to all constraints and guidelines outlined in this solicitation.

a. Human Factors and Performance Team

The Human Factors and Performance Team is studying ways to improve daily living and keep crewmembers and other personnel healthy, productive and safe during long duration exploration missions (LDEMs). Overall Team aims are to reduce performance errors and mitigate habitability, environmental and behavioral factors that pose significant risks to mission success. The Team develops guidelines for human systems design and information tools to support crew performance. Team members are examining ways to improve sleep and scheduling of work shifts as well as how specific types of lighting in the spacecraft and habitat can improve alertness and performance. Other projects address improving the interactions between automated and manual control of a spacecraft and how factors in the environment, such as dust in microgravity, can impact crew health. Team information, including the Team Executive Summary and research goals and priorities, is located at: <u>http://www.nsbri.org/science-and-technology/human-factors-and-performance</u>.

Proposals are solicited that address the research topic described below:

Operationalize Customized Refresher and Just-In-Time Training Products for Deep Space, Long Duration Spaceflight Crews

HRPRD Risks:

- Risk of Performance Errors Due to Training Deficiencies
- Risk of Inadequate Critical Task Design
- Risk of Inadequate Design of Human and Automation/Robotic Integration

IRP Gaps:

- **SHFE-TRAIN-01:** We do not know which validated objective measures of operator proficiency and of training effectiveness should be used for future long-duration exploration missions.
- **SHFE-TRAIN-03:** We need to develop guidelines for effective onboard training systems that provide training traditionally assumed for pre-flight.
- **SHFE-TASK-01:** How can workload measures and tools be developed to unobtrusively monitor and trend workload throughout the mission design and verification cycle in a consistent manner?
- **SHFE-HARI-03:** We do not know how to quantify overall human-automation-robotic system performance to inform and evaluate system designs to ensure safe and efficient space mission operations.

Background:

During LDEMs astronauts are certain to be faced with critical and complex tasks for which the crewmembers have either not been recently trained on, or have never been trained to execute. Moreover, in-flight crew hours are amongst the most precious resources during human spaceflight, so onboard training efficiency is of critical importance. Therefore a need exists to research how best to bring an inflight astronaut up to demonstrated competency to perform a complex and critical task, after a significant period has elapsed since final ground-training.¹

With the goal of future operational implementation NSBRI is interested in further refining existing novel or recently developed refresher or just-in-time training products. Improvements to these training products should lower both the resource footprint for generating mission relevant content, and the operational overhead for viewing such content.

Research Topic:

NSBRI is soliciting proposals to test and compare novel training products against conventional training products using metrics that measure both the resources needed to generate and implement each training product, and the performance of the subjects in executing tasks. These integrated products must be refined and customized for use with astronaut-like subjects and tested in a suitable ground analog environment such as NASA's Human Exploration Research Analog (HERA)² or equivalent facility. International collaborations that enable the use of ground analog facilities located in space-faring nations outside of the U.S. are encouraged. <u>This follow on integration and testing work must be able to be completed within a 12-month period.</u>

References:

- 1. <u>http://www.nsbri.org/projects/indivProject.asp?id=405&projID=362</u>
- 2. <u>http://www.nasa.gov/hrp/research/analogs/hera</u>

b. Musculoskeletal Alterations Team

The Musculoskeletal Alterations Team is studying the mechanisms involved in bone and muscle loss and whether reduced gravity increases the risk of bone breaks and impairs fracture healing. The Team is also researching radiation-induced bone loss. In addition to identifying ways to enhance the benefits of exercise during space flight for maintaining muscle and bone function, the Team is investigating methods to prevent or reduce the loss through nutritional and pharmaceutical interventions to complement exercise. Team information, including the Team Executive Summary and research goals and priorities, is located at:

http://www.nsbri.org/science-and-technology/musculoskeletal-alterations.

Proposals are solicited that address the research topic described below:

Customize, Refine, and Test Existing Exercise Software Product(s) to Optimize Astronaut Motivation for Exercise During Deep Space Exploration Missions.

HRPRD Risks:

- Risk of Impaired Performance Due to Reduced Muscle Mass, Strength and Endurance
- Risk of Reduced Physical Performance Capabilities Due to Reduced Aerobic Capacity
- Risk of Adverse Cognitive or Behavioral Conditions and Psychiatric Disorders

IRP Gaps:

- M7: Develop the most efficient exercise program for maintenance of muscle fitness.
- M9: Identify and validate exploration hardware for maintenance of muscle fitness.
- A7: Develop the most efficient exercise program for the maintenance of aerobic fitness.
- **BMed1:** We need to identify and validate countermeasures that promote individual behavioral health and performance during exploration class missions.

Background:

Recent analog studies (i.e., Mars500) have suggested that during LDEMs, astronauts may develop hypokinesis and therefore potentially have less time available to perform exercise at vigorous intensity levels.³ Diligently observing prescribed exercise schedules is critical to maintaining astronaut crew members' aerobic, musculoskeletal, and behavioral health during multi-year space missions, during which protracted 6-10 month periods may be spent on interplanetary transits in microgravity. A key factor in sustaining vigorous levels of exercise is maintaining high levels of motivation.

Recently, several researchers have begun to explore ways to motivate astronauts to be physically active at the levels necessary to mitigate the effects of bone and muscle loss, reduced aerobic capacity, and enhance behavioral health during spaceflight.⁴ These strategies that are designed to increase the motivation of crew members for exercise include the use of video exercise games. On Earth, such exercise video games have begun to find their way into the mainstream fitness marketplace as a way to increase people's motivation and enjoyment for exercise by being humorous, interesting, and above all by providing a means by which to interact with others who are "working out." Some of these exercise games also involve competition among the participants. NSBRI seeks to move these existing research products to higher technology and or countermeasure readiness levels by further refining them and testing them in appropriate ground

analog environments.

Research Topic:

NSBRI is soliciting research proposals that seek to modify, refine, and customize for astronaut use one or more existing exercise software products that are capable of autonomously administering exercise countermeasures to astronaut crew members. These software products will likely include the use of virtual exercise trainers, partners, or avatars. The analog definition studies should demonstrate a measureable improvement in crew members' physical conditioning, enjoyment and motivation for exercise during LDEMs, thereby maintaining aerobic, musculoskeletal, and behavioral health at optimal levels during simulated LDEMs. These technologies must be tested in a suitable ground analog such as the HERA. International collaborations that enable the use of ground analog facilities located in space-faring nations outside of the U.S. are encouraged. This follow on development and testing work must be feasibly completed within a one-year period.

References:

- 3. Basner, M., *et al* "Mars 520-d mission simulation reveals protracted crew hypokinesis and alterations of sleep duration and timing", *PNAS*, (2013), Feb 12, 110(7), 2635-40
- 4. <u>http://www.nsbri.org/projects/indivProject.asp?id=412&projID=337</u>

c. Neurobehavioral and Psychosocial Factors Team

The Neurobehavioral and Psychosocial Factors Team is concerned with methods crews utilize to deal with stress, isolation, confinement, and the challenges of LDEMs. In addition to identifying neurobehavioral and psychosocial risks to crew health, safety, and productivity, Team objectives include developing methods to monitor cognitive function and behavior and countermeasures to enhance performance, motivation, and quality of life. The Team's efforts also include projects conducted during the Mars 500 study in Russia and other analog environments. Team information, including the Team Executive Summary and research goals and priorities, is located at: http://www.nsbri.org/science-and-technology/neurobehavioral-and-psychosocial-factors.

Proposals are solicited that address the research topic described below:

Integrate Multiple Unobtrusive Technologies to Increase the Sensitivity and Specificity of Monitoring Psychosocial Well-Being and Alertness Levels in Astronaut-Like Subjects.

HRPRD Risks:

- Risk of Performance Decrements and Adverse Health Outcomes Resulting from Sleep Loss, Circadian Desynchronization, and Work Overload
- Risk of Adverse Cognitive or Behavioral Conditions and Psychiatric Disorders

IRP Gaps:

• Sleep Gap 1: We need to identify a set of validated and minimally obtrusive tools to monitor and measure sleep-wake activity and associated performance changes for spaceflight.

• **BMed2:** We need to identify and validate measures to monitor behavioral health and performance during exploration class missions to determine acceptable thresholds for these measures.

Background:

It is very challenging for high-performing and heroic individuals, such as astronauts, to admit that they are tired, stressed, emotionally upset, depressed, anxious, etc. Therefore unobtrusive means have been developed and tested to ensure that objective feedback regarding alertness levels and psychosocial well-being can be provided to the astronaut crew-members themselves, as well as to the mission commander and the flight surgeons (who are responsible for monitoring and treating the crew members). The unobtrusive technologies to monitor psychosocial wellbeing and alertness levels will be particularly useful during LDEMs since lengthy communications delays will require the crew to operate autonomously, without the constant intervention and availability of flight surgeons and behavioral experts.

Over recent years multiple technologies have been developed to:

- (1) Monitor alertness in astronauts; and
- (2) Unobtrusively observe the psychosocial well-being of astronauts.

Two examples of such technologies include Optical Computer Recognition or "OCR" (<u>http://www.nsbri.org/projects/indivProject.asp?id=419&projID=325</u>), and Lexical Indicators (<u>http://www.nsbri.org/projects/indivProject.asp?id=419&projID=339</u>). NSBRI has received advice that even more powerful technologies could be developed if existing products to monitor psychosocial well-being and/or alertness levels could be intelligently integrated or married together.

Research Topic

NSBRI is soliciting research proposals that with the goal of increasing sensitivity and improving specificity, combine two or more existing technologies that have been developed to monitor alertness levels and/or psychosocial well-being in astronaut-like subjects. Proposers must describe how they will refine and customize this integrated product for use with astronaut-like subjects and test it in a suitable ground analog environment (such as NASA's HERA or equivalent facility). International collaborations that enable the use of ground analog facilities in space-faring nations located outside of the U.S. are encouraged. This follow on integration and testing work must be able to be completed within a 12-month period.

d. Radiation Effects Team

The Radiation Effects (RE) Team is focused on understanding and mitigating the risks related to exposure to various types of space radiation. The NSBRI Center for Space Radiation Research (CSRR) is the central component of the Team with multiple projects addressing the effects of exposure from both solar particle events and galactic cosmic rays and better defining the risks to astronaut crew members. The CSRR, along with other RE projects, are identifying and validating possible countermeasures to prevent and mitigate the adverse health effects of space radiation. For example, EnteradeTM was recently tested as a possible countermeasure to ameliorate the acute effects of space-like radiation exposures. This research will have benefits for patients receiving radiotherapy as a medical treatment and as a treatment after accidental nuclear

radiation exposures. Team information, including the Team Executive Summary and research goals and priorities, is located at: <u>http://www.nsbri.org/SCIENCE-and-TECHNOLOGY/Radiation-Effects/</u>

Proposals are solicited that address the research topic described below:

Protect Healthy-Tissues from Ionizing Radiation by Accelerating the Testing of Potential Countermeasures in Human Clinical Research Trials

HRPRD Risks:

- Risk of Adverse Cognitive or Behavioral Conditions and Psychiatric Disorders
- Risk of Acute Radiation Syndromes Due to Solar Particle Events (SPEs)
- Risk of Cardiovascular Disease and Other Degenerative Tissue Effects From Radiation Exposure
- Risk of Acute and Late Central Nervous System Effects from Radiation Exposure

IRP Gaps:

- **BMed3:** We need to identify and quantify the key threats to and promoters of mission relevant behavioral health and performance during autonomous, long duration and/or long distance exploration missions.
- Acute 7: What are the most effective biomedical or dietary countermeasures to mitigate acute radiation risks?
- **Degen 6:** What are the most effective biomedical or dietary countermeasures to mitigate degenerative tissue risks? By what mechanisms are the countermeasures likely to work? Are these CMs additive, synergistic, or antagonistic to other Risks?
- **CNS 4:** What are the most effective biomedical or dietary countermeasures to mitigate CNS risks? By what mechanisms are the countermeasures likely to work?

Background:

Physical shielding from space radiation is not always feasible, particularly in protecting against high energy galactic cosmic rays (GCR) and unexpected solar particle events (SPEs). Hence, the development and validation of biological countermeasures is an important avenue to protect astronauts against the adverse effects of ionizing radiation during long-duration space travel. Countermeasures (e.g., pharmaceutical or medical foods) must be safe, clinically impactful, and have a long shelf-life in the space environment.

Countermeasures may be administered shortly after an SPE to mitigate against acute radiation effects. Countermeasures could also be taken for the entire duration of, and even after, spaceflight to protect against degenerative tissue effects. Late effects of ionizing radiation depend on complex chronic pathophysiological processes, which would be the likely targets of countermeasures against degenerative tissue effects. Therefore countermeasures utilized against chronic low-dose radiation may differ significantly from those effective against more acute radiation injury. Countermeasure dosing will depend mainly on mode of action and bioavailability.

The literature has indicated that countermeasures efficacious in terrestrial radiation exposure scenarios may also be of clinical utility for astronauts. For example, granulocyte colony

stimulating factor (G-CSF) was recently approved by the Food and Drug Administration (FDA) as the first (and only) countermeasure against acute radiation injury from a radiological or nuclear accident (Food and Drug Administration (2015) FDA approves Neupogen® for treatment of patients with radiation-induced myelosuppression following a radiological/nuclear incident).⁵ A pegylated form of this agent has shown beneficial effects in animal models of acute radiation effects from SPE-like protons.⁶ Other countermeasures are being tested in animal models.

FDA approved drugs are commonly used off-label in clinical settings. A handful of studies reported that some medications used off-label mitigated specific radiotoxic effects when tested in clinical trials with radiotherapy patients. Approved drugs have the advantage of established safety profiles, known side-effects, and well-defined mechanisms of action. Medical foods that meet these criteria and are comprised of components that are Generally Regarded as Safe (GRAS) have also shown promise in mitigating radiotoxicity in human and animal studies.^{7,8}

Medical radiotherapy for tumor ablation involves a high dose of gamma or proton radiation directed at a relatively small area, while the surrounding tissues receive a lower dose as a byproduct. For blood cancers such as lymphoma or leukemia where autologous bone marrow transplantation is performed, the patient receives whole body radiation fractionated over several days. In general, these types of exposures are quite different than the modalities and dose rates that astronauts experience during a LDEM. Moreover, radiotherapy patients typically receive additional treatments such as chemotherapy and display other health problems not relevant for astronauts. Despite these confounding issues, clinical studies in radiotherapy patients could augment ongoing animal model work and provide important additional human-based data regarding the efficacy of countermeasures for radiation-induced damage to flight surgeons caring for astronauts on LDEMs.

Ionizing radiation affects a plurality of organ systems. It is unreasonable to expect that one countermeasure will address all facets of radiation toxicity. Hence, the appropriate radiotherapy patient population should be emphasized in order to focus on certain tissue-specific defects associated with radiation exposure. Given the short timeline posed for the completion of the studies solicited in this NRA, patients and treatments that result in more acute toxicity which can be mitigated in a relatively short time-frame should be proposed. Specific outcomes should be noted and optimal dosing protocols should be determined.

Research Topic:

NSBRI is soliciting proposals that will test the efficacy of an FDA-approved medication (offlabel use is acceptable) or a medical food to mitigate acute radiotoxicity following radiation treatment in human patients. Proposers should investigate the use of suitable and well tolerated doses of the therapeutic agent. They should also characterize which negative outcomes of radiation exposure are prevented or ameliorated. Radiation exposures should be as space-like as possible, or alternatively, the use of high dose radiation should be well-rationalized. Tissues and acute toxicities of particular interest include: hematopoietic, gastrointestinal, and central nervous system (cognitive). Observations should be made of the biological systems that are unaffected by the therapeutic test agent as well as those that exhibit untoward changes. Finally, proposers should propose analytical schema that will relate as best as possible the terrestrial radiation exposure(s) to doses and dose rates that astronauts might experience during LDEMs. <u>These</u> studies must be able to be completed within a 12-month period.

References:

- 5. <u>http://www.fda.gov/EmergencyPreparedness/Counterterrorism/MedicalCountermeasures/</u><u>AboutMCMi/ucm443245.htm</u>.
- 6. Li et al. 2015. PLoS One. Vol. 10(3): e0120126. doi: 10.1371/journal.pone.0120126
- 7. Pietrofesa et al., 2014. J Pulm Respir Med. Vol. 4(6). pii: 1000215
- 8. Singh et al., J Radiat Res. 2013 Vol. 54(6): 973-88. doi: 10.1093/jrr/rrt048

e. Smart Medical Systems and Technology Team

The Smart Medical Systems and Technology Team is developing intelligent, integrated medical systems to assist in delivering quality health care during space flight on the ISS and LDEMs. These systems must be small, low-power, minimally invasive, versatile, and highly automated. Possible technologies needed include ultrasound diagnostics and therapeutics, lab-on-a-chip systems, patient and health physiologic monitors, and automated systems and devices to aid in medical decision making, training and diagnosis. New technologies developed by this Team will have immediate benefits to medical care on Earth. Team information, including the Team Executive Summary and research goals and priorities, is located at:

http://www.nsbri.org/SCIENCE-and-TECHNOLOGY/Smart-Medical-Systems-and-Technology/.

Proposals are solicited that address the research topic described below:

Employing a Suitable Ground Analog Environment, Develop and Test an Ultrasound Phantom or Surrogate Testing Capabilities to Enhance the Utility of Therapeutic Ultrasound

HRPRD Risks:

- Risk of Unacceptable Health and Mission Outcomes Due to Limitations of In-flight Medical Capabilities
- Risk Of Early Onset Osteoporosis Due To Spaceflight

IRP Gaps:

- ExMC 4.02: We do not have the capability to provide non-invasive medical imaging during exploration missions.
- ExMC 4.06: We do not have the capability to stabilize bone fractures and accelerate fracture healing during exploration missions.
- ExMC 4.08: We do not have the capability to optimally treat musculoskeletal injuries during exploration missions.
- ExMC 4.13: We have limited capability to screen for, diagnose, and treat renal stones during exploration missions.
- Osteo 5: We need an inflight capability to monitor bone turnover and bone mass changes during spaceflight.

Background:

NASA and NSBRI are partnering in the development of a flexible ultrasound system (FUS) that will provide broad ultrasound functionality to meet both the clinical diagnostic and therapeutic needs of astronaut crew members, as well as future research requirements during LDEM's. The FUS is briefly described by navigating to the following hyperlink: (http://www.hou.usra.edu/meetings/hrp2014/pdf/3082.pdf).

To assist with the demonstration and operational readiness of the FUS, high fidelity phantoms or surrogate validation systems are needed by NSBRI and NASA to reduce the need for research involving human test subjects, (thereby potentially significantly reducing the preparation and review time for these types of studies).

Research Topic:

NSBRI is soliciting research proposals that will develop and test portable, low maintenance ultrasound phantoms or surrogate testing setups to enable operational validation of the FUS for therapeutic applications in both laboratory and analog settings. Therapeutic applications include kidney stone movement and dissolution, bone fracture healing, bloodless surgery, maintenance of cartilage, etc. The research should involve the use of a suitable ground analog environment such as the HERA, or similar ground analog facility. International collaborations that enable the use of ground analog facilities in space-faring nations located outside of the U.S. are encouraged. This follow on development and testing work must be feasibly completed within a <u>one-year period</u>.

3. Career Development and Public Outreach

NSBRI has a Career Development and Outreach Program that operates in collaboration with other NASA programs to enhance and broaden public knowledge, understanding, and appreciation of biological and biomedical research, and the value of this research in the space environment. NSBRI's Career Development and Outreach Program is integrated with the NSBRI Science and Technology Program, as well as with collaborative research projects between NSBRI and NASA. Further information about NSBRI's Career Development and Outreach Program is available at: <u>http://www.nsbri.org/EDUCATION-and-TRAINING/</u>.

4. Vertebrate Animal Scientific Review

NASA has adopted the National Institute of Health (NIH) policy for all research proposals that require vertebrate animals, and requires that any and all research proposals that request funding for vertebrate animal research shall be reviewed as described in the Vertebrate Animal Scientific Review (VASR) as posted on the NSPIRES solicitation download site alongside this NRA. Each response to this solicitation that requires vertebrate animals must address the five points outlined in the VASR. The VASR requirements are in addition to Institutional Animal Care and Use Committee (IACUC) requirements as outlined under section B.2.b of the HERO Overview, Special Matters. All vertebrate animal research conducted under NSBRI auspices shall conform to the VASR requirement.

5. NASA Civil-Servant Investigators or Collaborators

Invited Step-2 research proposals entered in the NASA Solicitation and Proposal Integrated Review and Evaluation System (NSPIRES) system that include NASA civil servants will be required to provide complete information concerning percent effort and total dollar amount requested for each NASA employee listed in the proposal. NSBRI funding will be withheld if the following items are not included in the proposal a) SECTION VIII - OTHER PROJECT INFORMATION should capture the total full-time equivalents (FTE) for all NASA civil servants combined per year. For an FTE fraction, please use the format "0.xx"; b) SECTION X (Budget) – under F- OTHER DIRECT COSTS - for each budget period, list the name of each NASA civil servant on a separate line and specify total support (salary, materials, travel and equipment) for each individual; and c) in the BUDGET JUSTIFICATION section of the written proposal, itemize each fractional FTE and include the total dollar amount for salary, materials, travel and equipment per year per civil servant. Please contact the NSPIRES Help Desk at 202-479-9376 if you encounter any difficulties entering civil servant information.

6. NASA Safety Policy

Safety is NASA's highest priority. Safety is the freedom from those conditions that can cause death, injury, occupational illness, damage to or loss of equipment or property, or damage to the environment. NASA's safety priority is to protect: (1) the public; (2) astronauts and pilots; (3) the NASA workforce (including employees working under NASA instruments); and (4) high-value equipment and property. All research conducted under NSBRI auspices shall conform to this policy.

7. Availability of Funds for Award

NSBRI's obligation to make awards is contingent upon the availability of the appropriated funds from which payment can be made and the receipt of proposals that are deemed acceptable for award under this solicitation.

B. Award Information

All proposals will be evaluated for overall merit by independent peer-review panels and also will be assessed by NSBRI for relevance and proposed cost. Proposals to continue or supplement existing grants, if selected, will result in a new grant.

NSBRI will accept proposals with a maximum budget of \$400,000 per year for a maximum of one year. NSBRI reserves the right to return proposals that exceed \$400,000 per year or one year in duration. NSBRI does not provide separate funding for direct and indirect costs; thus, the amount of the award requested is the total of all costs submitted in the proposed budget.

NSBRI will make funding allocations in a single one-year increment based on the submitted budget, available funds and project review. All NSBRI award recipients will be reimbursed for expenses <u>incurred</u> in the one year performance period. NSBRI may withhold payment of any

expenditure that appears questionable, or for which additional information or support is required. A final report will be due at the conclusion of the one year funding period and final invoices will not be paid until this Annual Progress Report has been submitted, reviewed by the NSBRI Science Office and deemed acceptable. As specified in NSBRI's Cooperative Agreement Management Plan (CAMP) NASA-NSBRI customer-supplier agreements may also be required to be put in place, where appropriate.

NSBRI may, in certain cases, elect to fund only a portion of a proposed effort. In this case, the applicant will be given the opportunity to accept or decline such partial funding. The initial selection will be announced no earlier than April 2016. Once an award is made, NSBRI may elect to fund collaborating institutions participating in a given project directly. Budgets will then be required from each participating institution.

It is anticipated that NSBRI grants issued in response to this NRA will begin no earlier than May 2016. The grants will end by 31 May 2017. No extensions for these grants will be provided.

C. Eligibility Information

1. Eligibility of Applicants

All categories of United States (U.S.) institutions are eligible to submit proposals in response to this NRA. Principal Investigators may collaborate with universities, Federal Government laboratories, the private sector, and state and local government laboratories. In all such arrangements, the applying entity is expected to be responsible for administering the project according to the management approach presented in the proposal.

The applying entity must have in place a documented base of ongoing high quality research in science and technology, or in those areas of science and engineering clearly relevant to the specific programmatic objectives and research emphases indicated in this NRA. Present or prior NSBRI or NASA support of research or training in any institution or for any investigator is not a prerequisite for submission of a proposal.

2. Guidelines for International Participation

a. Guidelines for International Proposals

NASA's policy is to conduct research with non-U.S. organizations on a cooperative, no exchange-of-funds basis. Although Co-Investigators or collaborators employed by non-U.S. organizations may be identified as part of a proposal submitted by a U.S. organization, NSBRI funding through this NRA may not be used to support research efforts by non-U.S. organizations at any level; however, the direct purchase of supplies and/or services that do not constitute research from non-U.S. sources by U.S. award recipients is permitted. See NASA FAR Supplement Part 1835.016-70 for additional information on international participation, which can be referenced at http://www.hq.nasa.gov/office/procurement/regs/1835.htm#35_016-70.

Also see NASA Policy Directive 1360.2B Initiation and Development of International Cooperation in Space and Aeronautics Programs, which is located at http://nodis3.gsfc.nasa.gov/displayDir.cfm?Internal_ID=N_PD_1360_002B_&page_name=main

b. Assurance of Compliance – China Funding Restriction

All proposals submitted to this NRA must comply with the following: Assurance of Compliance with The Department of Defense and Full-Year Appropriation Act, Public Law 112-10 Section 1340(a); The Consolidated and Further Continuing Appropriation Act of 2012, Public Law 112-55, Section 539; and future-year appropriations herein after referred to as "the Acts", whereas:

- a) NSBRI and NASA are restricted from using funds appropriated in the Acts to enter into or fund any grant or cooperative agreement of any kind to participate, collaborate, or coordinate bilaterally with China or any Chinese-owned company, at the prime recipient level and at all sub-recipient levels, whether the bilateral involvement is funded or performed under a no-exchange of funds arrangement.
- b) Definition: "China or Chinese-owned Company" means the People's Republic of China, any company owned by the People's Republic of China, or any company incorporated under the laws of the People's Republic of China.
- c) The restrictions in the Acts do not apply to commercial items of supply needed to perform a grant or cooperative agreement.
- d) By submission of its proposal, the proposer represents that the proposer is not China or a Chinese-owned company, and that the proposer will not participate, collaborate, or coordinate bilaterally with China or any Chinese-owned company, at the prime recipient level or at any sub-recipient level, whether the bilateral involvement is funded or performed under a no-exchange of funds arrangement.

For a practical interpretation and application of these "China Funding Restrictions", proposers should carefully review the PRC FAQ for ROSES: http://science.nasa.gov/researchers/sara/faqs/prc-faq-roses/

c. Export Control Guidelines Applicable to Proposals Including Foreign Participation

Proposals including foreign participation must include a section discussing compliance with U.S. export laws and regulations, e.g., 22 CFR Parts 120-130 and 15 CFR Parts 730-774, as applicable to the circumstances surrounding the particular foreign participation. The discussion must describe in detail the proposed foreign participation and is to include, but not be limited to, whether or not the foreign participation may require the prospective investigator to obtain the prior approval of the Department of State or the Department of Commerce via a technical assistance agreement or an export license, or whether a license exemption/exception may apply. If prior approvals via licenses are necessary, discuss whether the license has been applied for or, if not, the projected timing of the application and any implications for the schedule. Information regarding U.S. export regulations is available at http://www.bis.doc.gov/.

3. Cost Sharing or Matching

NSBRI awards require a cost-sharing arrangement with all non-government entities consisting of an augmentation of at least 10% of the total annual NSBRI award. This contribution should not be identified in the submitted project budget but will be requested at the time the institutional award is made.

4. Data Accessibility

All research data resulting from NSBRI funded studies must be submitted to NSBRI Headquarters. These data will subsequently be archived in the NASA Life Sciences Data Archive (LSDA) (<u>http://lsda.jsc.nasa.gov/</u>) for the benefit of the greater research and operational spaceflight community. Archival data products may include but are not limited to low-level (raw) data, high-level (processed) data, meta-data, and data products such as calibration data, documentation, related software, and other tools or parameters that are necessary to interpret the data. Once a grant is awarded, the PI, NSBRI Science Office staff, and the supporting NASA HRP Element Scientist shall work with LSDA to outline specific archiving requirements in an LSDA Data Submission Agreement. These requirements shall include which data are to be included, the format of the data, and the timeframe in which the data is expected to be submitted for archiving.

5. Software Sharing Policy

NSBRI has adopted the National Institute of Health's (NIH) policy concerning the sharing of software produced through NSBRI grants. A software dissemination plan, with appropriate timelines, is expected in the application only if software development is a part of the application. There is no prescribed single use license for software produced through grants responding to this announcement. In accordance with federal law, NSBRI will protect the privacy and ownership rights of software developers. However, NSBRI does have goals for software dissemination, and reviewers will be instructed to evaluate the dissemination plan relative to these goals:

- 1. The software should be freely available to biomedical researchers and educators in the non-profit sector, such as institutions of education, research institutions, and government laboratories.
- 2. The terms of software availability should permit the dissemination and commercialization of enhanced or customized versions of the software, or incorporation of the software or pieces of it into other software packages.
- 3. To preserve utility to the community, the software should be transferable such that another individual or team can continue development in the event that the original investigators are unwilling or unable to do so.
- 4. The terms of software availability should include the ability of researchers to modify the source code and to share modifications with other colleagues. An applicant should take responsibility for creating the original and subsequent "official" versions of a piece of software.
- 5. To further enhance the potential impact of their software, applicants are expected to propose a plan to manage and disseminate the improvements or customizations of their

tools and resources by others. This proposal may include a plan to incorporate the enhancements into the "official" core software, may involve the creation of an infrastructure for plug-ins, or may describe some other solution.

The plan for software sharing will be evaluated during peer review together with any other resource sharing plans.

The adequacy of the software sharing plans will be considered by NSBRI when making recommendations about funding applications as appropriate. In making such considerations, prior to funding, NSBRI may negotiate modifications of software sharing plans with the Principal Investigator. Any software dissemination plans represent a commitment by the institution (and its subcontractors as applicable) to support and abide by the plan.

D. Proposal and Submission Information

1. Source of Application Materials

All information needed to submit an electronic proposal in response to this announcement is contained in this NRA and in the companion document entitled "Guidebook for Proposers Responding to a NASA Research Announcement (NRA)" (hereafter referred to as the *Guidebook for Proposers*) that is located at:

http://www.hq.nasa.gov/office/procurement/nraguidebook/.

Additionally, applicants shall prepare proposals in accordance with the "Instructions for Responding to NASA Research Announcements," NASA Federal Acquisition Regulations (FAR) Supplement (NFS), Part 1852.235-72 (November 2004), hereafter referred to as the *NASA FAR Supplement*, that is located at:

http://www.hq.nasa.gov/office/procurement/regs/5228-41.htm#52_235-72.

The information in this NRA **supersedes** and provides additional direction to that found in the *Guidebook for Proposers* and provides additional direction consistent with the *NASA FAR Supplement*. Proposals that do not conform to the standards outlined in this solicitation will be declared noncompliant and will be handled in accordance with the *NASA FAR Supplement*.

Proposal submission questions received will be answered and published in a Frequently Asked Questions (FAQ) document. This FAQ will be posted on the NSPIRES solicitation download site alongside this NRA, and will be updated periodically between submission release and the Step-2 proposal due date. Any supplemental information will also be posted alongside this NRA.

2. Content and Form of Proposal Submission

a. Registration in NASA Proposal Data System

This NRA requires that the proposer register key data concerning their intended submission with the NASA Solicitation and Proposal Integrated Review and Evaluation System (NSPIRES)

located at <u>http://nspires.nasaprs.com</u>. Potential applicants are urged to access this site well in advance of the proposal due date(s) of interest to familiarize themselves with its structure and enter the requested identifier information. It is especially important to note that every individual named on the proposal's *Cover Page* (see further below) must be registered in NSPIRES and that such individuals must perform this registration themselves. Team members will be asked to confirm their organization affiliation when added to a proposal. No one may register a second party, even the Principal Investigator (PI) of a proposal in which that person is committed to participate. This data site is secure and all information entered is strictly for NASA's use only.

Every organization that intends to submit a proposal to NSBRI in response to this NRA, including educational institutions, industry, nonprofit institutions, NASA Centers, the Jet Propulsion Laboratory, and other U.S. Government agencies, **must be registered in NSPIRES**, regardless of the electronic system used to submit proposals. Such registration must be performed by an organization's electronic business point-of-contact (EBPOC) in the Central Contractor Registry (CCR).

b. Electronic Submission

Proposals must be submitted electronically. Step-1 and Step-2 proposals must be submitted electronically by one of the officials at the PI's organization who is authorized to make such a submission. All team members must be registered in NSPIRES and confirm their organizational affiliation when added to a proposal before the PI organization official can submit. It is strongly recommended that the PI work closely with his/her team members and organization official to ensure the proposal is submitted by the due date and time listed in this solicitation. Proposals submitted after the listed due dates and times will be will be declared noncompliant and will be handled in accordance with the NASA FAR Supplement.

NSBRI Step-1 proposers must use NSPIRES for proposal submission. All proposers, team members, and agency officials must be registered before proposal submission with NSPIRES regardless of the electronic system used to submit proposals. NSPIRES remains the only system through which a Step-1 proposal can be continued as a Step-2 proposal. Proposers submitting a Step-1 proposal who receive an invitation to submit a Step-2 proposal will have the option of building on a stored Step-1 proposal within the NSPIRES database. All invited proposers must use NSPIRES for Step-2 proposal submission.

NSPIRES accepts fully electronic proposals through a combination of data-based information (e.g., the electronic *Cover Page* and its associated forms) and uploaded PDF file(s) that contain the body of the proposal. The website will provide a list of all elements that make up an electronic proposal, and the system will conduct an element check to identify any item(s) that is(are) apparently missing or incomplete. Proposers are particularly encouraged to begin their submission process early.

Requests for assistance in accessing and/or using this Website may be directed by E-mail to <u>nspires-help@nasaprs.com</u> or by telephone at 202-479-9376 Monday through Friday, 8:00 AM – 5:00 PM Eastern Time. Frequently Asked Questions (FAQs) may be accessed through the

Proposal Online Help site at <u>http://nspires.nasaprs.com/external/help.do</u>. Tutorials of NSPIRES are available at <u>http://nspires.nasaprs.com/tutorials/index.html</u>.

3. Intent to Propose and Step-1 Proposals

Proposals solicited through this NRA will use a 2-Step proposal process for which the Notices of Intent (NOI) take the form of a required Step-1 proposal.

The NSPIRES system will guide proposers through submission of all required proposal information. Please note that the Proposal Summary, Business Data, Program Specific Data, and Proposal Team are required Cover Page Elements for a Step-1 proposal. The proposal summary should be between 100-300 words (4000 characters maximum) and understandable by the layman reader. Budgets should not be included with the Step-1 proposal. The project team is not considered binding for Step-1 and can be adjusted in an invited Step-2 proposal. Failure to include any of the key components may result in return of your Step-1 proposal without review.

To initiate a Step-1 proposal:

- Log in using your NSPIRES user name and password.
- Click on Proposals under the NSPIRES Options.
- Click on the Create Proposal button in the upper right hand corner of the screen.
- Select "Solicitation" to prepare a new proposal.
- Click the button for "Appendix B: NSBRI Research and Technology Development to Support Crew Health and Performance in Space Exploration Missions" (NNJ15ZSA001N-NSBRI).
- Follow the step-by-step instructions provided in NSPIRES to complete your Step-1 proposal.

Step-1 proposals submitted to NSBRI will include a synopsis of the intended research, with the total length of the proposal not to exceed five 8 ½ by 11 inch pages using a standard 12-point font and one inch margins. This synopsis will be provided as a PDF proposal document upload, and must not be password protected or locked in any way. **Required elements** of the five-page, Step-1 application include:

- (1) a proposed NSBRI team assignment
- (2) a clear indication of the relevance to one or more of the research emphases (Section A.2.a-f)
- (3) a plan outline for countermeasure(s) and/or technology development (including approach and key personnel)
- (4) the project impact
- (5) the rationale for the significance of the proposed research in mitigating risks associated with human exploration of space
- (6) the Earth-based applications, and if applicable, commercialization potential.

No additional documents should be uploaded with the Step-1 proposal. Budget and detailed

program data should not be included with the Step-1 proposal. Project personnel are not considered binding for Step-1 and can be adjusted in an invited Step-2 proposal. References are not required for the Step-1 proposal, and if included, count towards the 5-page limit.

If your proposal is a resubmission, you should identify it as such in your Step-1 submission; you are not, however, required to address prior reviews unless invited to submit a full proposal. Please be aware that submission of a Step-1 proposal to re-introduce a proposal invited during a previous review cycle to submit as a Step-2 proposal, but not funded (i.e. a re-submission from a previous round of review), does not guarantee that this newly submitted Step-1 proposal will necessarily be judged as responsive to the areas of focus in the current NRA and therefore invited to submit as a Step-2 proposal.

Step-1 proposals are prepared by the PI or a designated representative of the PI. Step-1 proposals are submitted by an official of the PI's organization after the PI has released the prepared proposal to the institution official. It is strongly recommended that the PI work closely with his/her organization official to ensure the proposal is submitted by the due date and time listed in this solicitation. Proposals will not be accepted after the listed due dates except for as provided in the NASA FAR Supplement 1852.235-72(g).

Step-1 proposals shall be electronically submitted by the due date and time listed in Section G. Electronic submission of Step-1 proposals will be open during the period listed in Section G.

All submitters of Step-1 proposals must log in to NSPIRES on or after the Step-1 notification date listed in Section G to receive their Step-2 full proposal invitation status. A courtesy email will be generated by NSPIRES as a reminder to check full proposal invitation status; however, it is the responsibility of the submitter to log in to NSPIRES to receive their full proposal invitation status.

Decision information can be accessed in two ways:

- After logging in, the PI selects the "Proposals" link, the "Submitted Proposals/NOIs" link, and then clicks on the proposal submitted to the solicitation identified above. The document(s) provided by NASA will be displayed under the heading "PI Information Package" located at the bottom of the "View Proposal" page.
- 2) After logging in, the Authorized Organization Representative selects "Organization Mgmt" link and, from within the submitting organization, selects the "Organization Proposals" link, the "Submitted Proposals" link and then clicks on the proposal submitted to the solicitation identified above. The document(s) provided by NASA will be displayed under the heading "PI Information Package" located at the bottom of the "View Proposal" page.

4. Instructions for Preparation of Invited Step-2 Proposals

Step-2 proposals are due by the due date and time listed in Section G. **Step-2 proposals will be accepted from invited proposers only.** Invited Step-2 proposals must be submitted through the

NSPIRES system.

The NSPIRES system will guide proposers through submission of all required proposal information. Select **prior-phase proposal** when creating an invited Step-2 proposal. Please note that the Proposal Summary, Business Data, Budget, and Proposal Team and Program Specific Ouestions are required Cover Page Elements for all Step-2 proposals. The proposal summary should be between 100-300 words (4000 characters maximum) and understandable by the layman reader. In addition to the Cover Page online budget forms, proposers are encouraged to provide expanded budgets as needed (i.e. subcontracts) as part of their budget justification (see number 11 below and the Guidebook for proposers). For proposals with NASA civil servant team members only: Proposers are required to enter the NASA civil servant team member name and fraction of full-time equivalent (FTE) involvement in the same field under the Item column in section F "Other Direct Costs" of the online budget. The funds requested should be entered as the Total Requested Funds for the NASA civil servant, including salary, fringe, materials, travel, etc. (see the FAQ posted alongside this document for additional budget instruction). This budget entry should be made for each year of NASA civil servant involvement, and is in addition to the agency identification under the team member section and the NASA civil servant FTE designation under the business data section.

To ensure proper Step-2 proposal transmission, please provide only **one** PDF attachment upload ordered as below. **For proposal sections 2 through 9 and section 17, specific instructions are given in this NRA (see section D.4.a though D.4.g). These specific instructions supersede those found in the NASA Guidebook for Proposers. Proposals that do not conform to these requirements may be declared noncompliant and declined without review.** For sections 10-16, proposers are encouraged to reference the NASA Guidebook for Proposers; however, there are no specific submission compliance requirements for these sections (format, structure, page counts, etc.).

- 1. Table of Contents
- 2. If applicable, inclusion of the Flight Experiment Resource Worksheet, or Analog Study Resource Worksheet.
- 3. Software Sharing Plan, if applicable.
- 4. Map to HRP Integrated Research Plan (IRP) (see D.4.a below).
- 5. Animal Care or Human Subjects certifications, if applicable (see D.4.b below).
- 6. Response to prior review, if applicable (see D.4.c below).
- 7. Productivity of currently funded research, if applicable (see D.4.d below).
- 8. Vertebrate Animal Scientific Review, if applicable (see D.4.e below and VASR posted on NSPIRES solicitation site).
- 9. Scientific or Technical Project Description (see section D.4.f below).
- 10. References and Citations.
- 11. Management Approach (see Guidebook for Proposers).
- 12. Personnel Curriculum Vitae (CV's) (see Guidebook for Proposers).
- 13. Current and Pending Support (see Guidebook for Proposers).
- 14. Facilities and Equipment (see Guidebook for Proposers).
- 15. Budget Justification of Proposed Costs (see Guidebook for Proposers).
- 16. Letters of Collaboration or Support.

17. Appendices or Reprints (See D.4.g below).

While the NSPIRES system allows for the upload of supporting documents as separate uploads, please provide the information above in only one PDF proposal document upload. It is essential that all PDF files generated and submitted meet NASA requirements. At a minimum, it is the responsibility of the proposer to:

- 1) ensure that all PDF files are unlocked and that edit permission is enabled this is necessary to allow NSPIRES to concatenate submitted files into a single PDF document; and
- 2) ensure that all fonts are embedded in the PDF file and that only Type 1 or TrueType fonts are used. In addition, any proposer who creates files using TeX or LaTeX is required to first create a DVI file and then convert the DVI file to Postscript and then to PDF.

See <u>http://nspires.nasaprs.com/tutorials/PDF_Guidelines.pdf</u> for more information on creating PDF documents that are compliant with NSPIRES.

There is a recommended 10 MB size limit for proposals (Section 2.3(c) of the NASA Guidebook for Proposers). Large file sizes can impact the performance of the NSPIRES system. Most electronically submitted proposals will be less than 2 MB in size.

NSPIRES accepts electronic proposals through a combination of data-based information (e.g., the electronic Cover Page) and the uploaded PDF file that contains the proposal as outlined above. The NSPIRES proposal submission process ensures that a minimum set of required proposal cover page fields are completed. Provision of the proposal summary and business data elements of the cover page will be necessary in order for the Authorized Organizational Representative (AOR) to submit the proposal to NASA. If either of these two proposal elements is incomplete, the "View Proposal/ Check Elements" function of NSPIRES will display red "error" flags and messages to alert the user to the information that is required but missing, and the "Submit Proposal" button will not be available. Although the PI will be able to release the proposal to the AOR, the proposal cannot be submitted by the AOR to NASA until these required fields are complete. Any additional information that is missing will be identified by yellow "warning" flags. Proposers are reminded to check the solicitation instructions to ensure compliance with all instructions, as adherence to these two element validation checks alone is insufficient to guarantee a compliant proposal. Additionally, in those cases where instruction in the NRA contradicts an NSPIRES warning, the NSPIRES yellow "warning" may be ignored. Proposers should follow the NRA instructions closely to help ensure submission of a compliant proposal.

The NSPIRES system is limited in the character sets that can be used in filling out on-line forms. Please refer to the on-line tutorials when using special characters. Alternatively, spell out special characters where possible (such as micro rather than the Greek symbol). Applicants are encouraged to preview their proposal prior to releasing the proposal to their designated Organization by clicking the "Generate" button at the bottom of the View Proposal Screen in NSPIRES. The "Generate" feature allows applicants to preview their entire proposal in a single PDF file prior to submittal, but it is not a required step in the submission process. Please contact

the NSPIRES Help Desk for assistance with this feature (e-mail <u>nspires-help@nasaprs.com</u> or by telephone at 202-479-9376).

a) Human Research Program Human Research Roadmap

The investigator must examine and understand the research emphases outlined in this NRA and the risks identified in the HRP Human Research Roadmap (HRR) (http://humanresearchroadmap.nasa.gov). Proposers must include a description as part of their proposal of how their research aims map to the identified IRP risks, gaps and deliverables. This description is limited to two pages and does not count towards the 20-page limit of the project description.

b) Special Matters

For proposals employing human subjects and/or animals, assurance of compliance with human subjects and/or animal care and use provisions is required.

Policies for the protection of human subjects in NASA sponsored research projects are described in NASA the NASA Policy Directive (NPD) 7100.8E "Protection of Human Research Subjects" (http://nodis3.gsfc.nasa.gov/displayDir.cfm?t=NPD&c=7100&s=8E)

Animal use and care requirements are described in the NASA Code of Federal Regulations (CFR) 1232 (<u>http://www.gpo.gov/fdsys/granule/CFR-2012-title14-vol5/CFR-2012-title14-vol5/part1232/content-detail.html</u>).

NASA utilizes a just-in-time practice for approval of the use of human subjects or animals. If the IRB/IACUC certification is already approved at proposal submission, attach a copy of the certification as part of the proposal.

After award, a statement must be provided from the Applicant institution which identifies the selected proposal by name and which certifies that the proposed work will meet all Federal and local requirements for human subjects and/or animal care and use. This includes relevant documentation of Institutional Review Board (IRB) approval and/or approval by the Institutional Animal Care and Use Committee (IACUC). NASA will require current IRB and IACUC certification prior to each year's award.

For delivery of any certifications received after the proposal due date, please contact Kevin Willison, Senior Scientist, NASA Research and Education Support Services, at kwillison@nasaprs.com.

c) Revised Proposals

Investigators submitting a proposal in response to this solicitation, and whose most recent submission that included similar specific aims to any NASA or NSBRI sponsored research announcement was not accepted, are required to submit an explanation of how the current proposal addresses criticisms from previous review cycles. This explanation shall be presented preceding the research description as part of the main proposal upload and is limited to two pages. This explanation should include changes to the current proposal as a result of review comments and/or explanation as to why prior review comments are not applicable to the current proposal.

Investigators resubmitting a proposal in response to this solicitation may only submit a proposal with similar hypothesis(es) and aims a total of three times (original submission plus two resubmissions). Significant changes must be made to the proposal hypothesis(es) and specific aims for consideration after the third attempt or the proposal will be declined without further review.

These two pages are not considered part of the 20-page project description. Proposal reviewers will be provided with the evaluations of prior submissions. Proposers must respond to prior criticisms relevant to any portion of the new proposal under consideration. Proposers who have questions concerning their response to a prior review are encouraged to contact Kevin Willison, Senior Scientist, NASA Research and Education Support Services, at kwillison@nasaprs.com.

d) Productivity of NASA- or NSBRI-Funded Research

Proposers currently funded by or who have received funding within the last three (3) years from NASA or NSBRI must provide specifics to the productivity of the supported research including progress in experiments, completion of milestones and deliverables, research publications, and new findings. This explanation should be presented preceding the research description as part of the main proposal upload and is limited to two pages. These two pages are not considered part of the 20-page project description. Related impacts to the proposed research plan, if any, should be highlighted in the body of the project description. **Proposers that request continued support that do not include this productivity section will be returned to the submitter without panel review and will not be considered for funding.**

e) Vertebrate Animal Scientific Review (if applicable)

Each response to this solicitation that requires vertebrate animals must address the five points outlined in the Vertebrate Animal Scientific Review (VASR) instructional document posted alongside this NRA. This response should be presented as part of the main proposal upload and is limited to two pages. These two pages are not considered part of the 20-page project description. A sample VASR is provided in the VASR instructional document.

f) Scientific/Technical/Management Section (Project Description)

The length of the project description of the proposal shall not exceed 20 pages using standard (12 point) type. Text shall have one-inch margins. Referenced figures and tables must be included in the 20 pages of the project description; however, figure captions can use a 10-point font. The proposal shall contain sufficient detail to enable reviewers to make informed judgments about the overall merit of the proposed research and about the probability that the investigators will be able to accomplish their stated objectives with current resources and the resources requested. The hypotheses (if appropriate) and specific aims of the proposed research shall be clearly stated. If applicable, a statistical section with proper justification should be included in the project description. **Proposals that exceed the 20-page limit for the project description (inclusive of ALL figures and tables) will be declared noncompliant and will be handled in accordance with Appendix A. Cited literature and all other proposal sections are not considered part of the 20-page project description. Reviewers are not required to consider information presented**

as appendices or to view and/or consider Web links in their evaluation of the proposal.

g) Reprints and Appendices

Reprints and Appendices, if any, do not count toward the project description page limit, and are to be included following all other sections of the proposal (reviewers are not required to consider information presented in proposal appendices).

E. Proposal Evaluation Process

1. Step-1 Proposal Relevancy Review

Each Step-1 proposal will be reviewed by members of the Institute's Executive Science and Medicine Council (ESMC). The ESMC will incorporate advice from NASA, and determinations of relevancy will be made, from which a final composite recommendation of "relevant" or "not relevant" will be made based upon research emphases outlined in Section A.2. Only those Step-1 proposals having a final evaluation of "relevant" will be invited to submit a full Step-2 proposal.

2. Step-2 Proposal Intrinsic Scientific and Technical Merit

To be responsive to this research solicitation, proposed studies should produce research product(s) that address the research emphases stated in this solicitation, and lead to new knowledge within accepted scientific and technology standards.

All of the following criteria will be used in determining the merit score.

Significance:

Does this study address a research emphasis stated in this solicitation? Does the study test a significant hypothesis or produce data that would enable a significant hypothesis to be generated? If the study is non-hypothesis driven, are the data produced needed to understand or reduce the risk addressed by the research emphasis? If the task will produce a software model or tool, how will it serve to better quantify or mitigate a risk? If the aims of the application are achieved, how well will the product(s) address the research emphases? If the aims of the application are achieved, how will scientific knowledge or technology advance?

Approach:

Are the conceptual framework, design, methods, and analyses adequately developed, well integrated, and appropriate to the aims of the project? Is the proposed approach likely to yield the desired results? Does the applicant acknowledge potential problem areas and consider alternative tactics?

Statistical Plan:

Does the study provide adequate justification for sample size? For example, is the choice of primary outcome relevant for the stated Aims? Are assumed effect magnitudes reasonable? Are assumed variability estimates reasonable? Are they estimated properly? Are they relevant for the proposed experimental design and data analysis methodology? What Type I and Type II errors are assumed? Is there room for a tradeoff here to accommodate sample size constraints and still provide useful information from the study? Do the investigators provide a reasonable data analysis plan? For example, is it appropriate for the proposed experimental design (e.g. repeated measures)? Does it address research hypotheses or aims? Is it robust to the sampling and other constraints associated with the research venue?

Risk Mitigation:

For a study quantifying risks to crew health or performance; does the study adequately improve the understanding of the adverse consequences, the probability of its occurrence, or the timeframe in which the risk must be addressed? For a study developing countermeasures, will the proposed countermeasure reduce a risk to crew health or performance, reduce the impact of the risk or reduce the resources required to mitigate it? For a study developing technology, will the research product reduce the risk to crew health or performance, reduce its impact or better define it and is the technology feasible within the confines of the operational environment?

Investigators:

Are the investigators appropriately trained and well suited to carry out this work? Is the work proposed appropriate to the experience level of the principal investigator and any co-investigators? Is the evidence of the investigators' productivity satisfactory?

Environment:

Does the scientific environment in which the work will be performed contribute to the probability of success? Do the proposed experiments take advantage of unique features of the scientific environment or employ useful collaborative arrangements? Is there evidence of institutional support?

3. Step-2 Proposal Review and Selection Processes

a. Compliance Matrix

All proposals must comply with the general requirements of the NRA as described in this solicitation, the *Guidebook for Proposers*, and the *NASA FAR Supplement*. Upon receipt, proposals will be reviewed for compliance with these requirements including:

- 1) Proposals will not be accepted after the due dates and times listed in this announcement except for as provided in the *NASA FAR Supplement*.
- 2) The proposal project description must be no more than 20 pages in length, (including all tables and figures).
- 3) Submission of appropriate IRB or IACUC certification for all proposals using human or animal test Subjects in accordance with the Special Matters requirements listed in section D.4.b.

- 4) Submission of an appropriate and justified budget for a funding period not exceeding that described in the NRA.
- 5) Investigators who are submitting a proposal in response to this solicitation, and whose most recent submission that included similar specific aims to any NASA or NSBRI sponsored research announcement was not accepted, are required to submit an explanation of how the current proposal addresses criticisms from previous review cycles. This explanation should be presented in a separate form of no more than two pages. Related changes to the research plan should be highlighted in the body of the project description as described in section D.4.c.
- 6) A description of how the research aims map to the identified IRP risks and gaps as described in section D.4.a.
- 7) A description that provides specifics to the productivity of the previously supported research including progress in experiments and research publications and new findings as described in section D.4.d.
- 8) Proposals that require vertebrate animals must include a Vertebrate Animal Scientific Review component as outlined in the VASR, not to exceed two pages.
- 9) For flight proposals, submission of the Flight Experiment Resource Worksheet.

10) Submission of any required analog definition forms.

11) If applicable, inclusion of the Analog Study Resource Worksheet.

12) Submission of all other appropriate information as required by this NRA.

Note: At NSBRI's discretion, non-compliant proposals may be withdrawn from the review process and declined without further review. Compliant proposals submitted in response to this NRA will undergo an intrinsic scientific or technical merit review. Only those proposals most highly rated in the merit review process will undergo additional reviews for program balance and cost.

b. Scientific and Programmatic Reviews

The overall evaluation process for proposals submitted in response to this NRA will include a First Tier Merit Review and a Second Tier Program Alignment Review. The **First Tier Review** will be a merit peer review by a panel of scientific or technical subject matter experts. The number and diversity of experts required will be determined by the response to this NRA and by the variety of disciplines represented in the proposals relevant to the research emphases described in this NRA. The merit review panel will assign *a score from 0-100, or assign a Not Recommended for Further Consideration (NRFC)* based upon the intrinsic scientific or technical merit of the proposal. The final score or NRFC designation will reflect the consensus of the peer review panel. After the merit review is complete the panel will be asked to include in their critique of each proposal any comments they may have concerning the proposal's budget. Proposals that are highly rated in the merit review process will undergo a **Second Tier Review** for program alignment.

For research requiring vertebrate animals, the first tier review will also include a VASR as outlined in the VASR posted on the NSPIRES solicitation download site alongside this NRA.

In addition, analog definition proposals and flight definition proposals will undergo reviews for feasibility as described below.

For NSBRI, a separate evaluation for program balance and proposed project cost will be performed. Evaluation of the cost of a proposed effort includes consideration of the reasonableness of the proposed cost. Programmatic balance will include an evaluation of how the proposed work may help achieve an appropriate balance of team, scientific and technical tasks in alignment with the IRP and the NSBRI missions. In accordance with the NIH policy that NSBRI has adopted, all applications will also be reviewed with respect to:

- Adequacy of plans to include males and females, members of minority groups, and their subgroups, as appropriate for the scientific goals of the research;
- Plans for the recruitment and retention of subjects;
- Reasonableness of the proposed budget and duration in relation to the proposed research;
- Adequacy of the proposed protection for humans, animals or the environment to the extent they may be adversely affected by the project proposed in the application.
- For proposals requiring vertebrate animals, coding of the VASR rated as Acceptable. NSBRI staff will work with the applicant to resolve concerns prior to award. <u>Coding of</u> <u>the VASR as Acceptable is required prior to award</u>.

The NSBRI User Panel (UP) will review those Step-2 proposals in the fundable range for operational relevance and feasibility. A set of selection recommendations will be developed by the NSBRI External Advisory Council (EAC) based on the merit review scores, programmatic balance, recommendations from the UP, and costs. These recommendations will be reviewed with NASA prior to selection by the NSBRI Director.

c. Analog Definition Proposals

Only those analog definition proposals that are most highly rated in the merit review process will undergo additional reviews for analog feasibility. A panel of technical experts from NASA will evaluate the feasibility of carrying out the analog experiment and the potential for establishing teams of investigators to optimize utilization of human subjects, samples, data, and analog resources. This review will be conducted by technical experts familiar with the development and conduct of analog studies.

d. Selection

The information resulting from these two levels of review, as described above, will be used to prepare selection recommendations developed by the NSBRI EAC. Selection for funding will be made by the respective selecting official identified in the Submission section of this NRA.

In order to optimize resources, NASA and NSBRI pursue the intentional formation of investigator partnerships between individual investigators whose experiments will leverage resources by addressing different facets of the same questions. NASA anticipates that such intentional teaming arrangements will result in better utilization of available resources to resolve specific critical questions. NASA and NSBRI strongly encourage investigators submitting

applications in response to this NRA to consider identifying collaborations between individual investigators as part of the development of their individual proposals and to identify this precoordination in their management plan. Additional information can be referenced in the NASA FAR Supplement. Finally, NASA and NSBRI may integrate proposals if, in their judgments, the goals, objectives or products of the proposals are similar.

For some NASA and NSBRI research topics, NASA is considering utilizing individual research proposals to form a Virtual NASA Specialized Center of Research (VNSCOR) where NASA aligns a set of individual awards into an NSCOR-like team project. Individual proposals may be selected to become Elements of a VNSCOR. Elements of the VNSCOR will also join a working group organized by NASA on the specific research topic. VNSCORs will be composed of four to six individual research elements, each with its own specific aims.

Where appropriate for analog definition studies, NSBRI and NASA reserve the right to form teams of investigators whose experiments have compatible requirements for human subjects, specimens, operations, data, and treatment and sharing of biological samples. A selected investigator who becomes a member of a research team will be required to work with other team members to develop an integrated set of objectives that can be met within fiscal and analog or flight resource constraints. Development of this integrated approach may result in modification, transfer, addition or deletion of some objectives put forth in an individual proposal. Specifics associated with the definition period will be addressed with the investigator at the time of selection.

Additionally, proposals submitted in response to this solicitation found to have strong programmatic relevance and scientific merit that cannot be funded due to limited resources may be forwarded to partner programs or agencies for consideration. NASA reserves the right to select proposals submitted to NSBRI that NSBRI does not select; such a selection will result in the award of a NASA grant. Similarly, NSBRI reserves the right to select proposals submitted to NASA that NASA does not select; such a selection will result in the award of a NSBRI grant. In these instances, the PI will be given the opportunity to accept or decline the offer.

f. Ombudsman

Resolution of concerns during the pre-award and post-award phases of this solicitation is under the auspices of the NSBRI Chief Scientist, Dr. Graham B.I. Scott (ph. 713-798-7227; fax 713-798-7413; email: <u>Graham.Scott@bcm.edu</u>).

F. Award Administration Information

1. Award Notices

At the end of the selection process, each Step-2 proposing organization will be notified of its selection or non-selection status. NSBRI will provide debriefings to those investigators who request one. Selection notification will be made by a letter signed by the designated NSBRI selecting official. The selection letters are not an authorization to begin performance. The

selected organization's business office will be contacted by a representative of the NSBRI to negotiate an award. Any costs incurred by the investigator in anticipation of an award are at their own risk until contacted by NSBRI. NSBRI will determine the type of award instrument, request further business data, and negotiate the resultant action. NSBRI awards will be issued and funded by NSBRI. NSBRI reserves the right to offer selection of only a portion of a proposal. In these instances, the investigator will be given the opportunity to accept or decline the offer.

2. Administrative and National Policy Requirements

All grant awards are subject to the provisions detailed in 2 CFR Parts 200 and 1800 (i.e., for higher education, hospital, and non-profit entities) and 14 CFR 1274 (i.e., for commercial firms).

3. Individual Researcher Reporting

a. Intellectual Property Reporting

Institutions awarded NSBRI funding must report each invention disclosure or patent application resulting from their NSBRI research grant to **both** NSBRI and NASA within 60 days of investigator disclosure to the home institution.

For NASA: Submit either a hard copy of Form 1679 (see <u>https://invention.nasa.gov/assets/downloads/nf1679.doc</u>) to NASA Innovative Partnerships Office, Mail Code AF2, 2101 NASA Parkway, Houston, TX 77058 OR submit online at <u>https://ntr.ndc.nasa.gov</u>. In the field designating contract number, please cite NCC 9-58.

For NSBRI: In addition to reporting on intellectual property on the annual project report, please also send copies of the institutional invention disclosure AND NASA Form 1679 or the summary from the online disclosure at <u>https://ntr.ndc.nasa.gov</u> via email to <u>info@nsbri.org</u>.

b. Final Report

A final report must be provided to the NSBRI at the end of the 12 month funding period, including a detailed listing of all peer-reviewed publications. The final report is a requirement for eligibility for future NASA/NSBRI solicitations as well as for the payment of final invoices. This report is due 60 days post the conclusion of the funding period.

A component of this final report will be used for the NASA Space Life & Physical Sciences Research & Applications Division Task Book (https://taskbook.nasaprs.com/Publication/welcome.cfm). The Task Book includes descriptions of all peer-reviewed activities funded by the Human Exploration and Operations Mission Directorate (HEOMD). The Task Book is an invaluable source of information for NSBRI and NASA biological and biomedical researchers as well as the external scientific and technical communities. This information will consist primarily of:

- an abstract;
- a bibliographic list of publications;
- invention disclosures;
- a statement of progress, including a comparison with the originally proposed work schedule;
- results of periodic data reviews

The information in this final report will consist primarily of:

- statement of the specific objectives;
- significance of the work;
- background;
- overall progress during the performance period;
- narrative discussion of technical approaches including problems encountered;
- accomplishments related to approach; and
- an appendix with bibliography, copies of all publications and reports, and intellectual property disclosures. Any publications or other public materials containing data are particularly important to include in this section.

c. Publications

For NSBRI-funded research, please clearly identify support received from the National Space Biomedical Research Institute in all publications, invention disclosures, copyrights and patents, using the following phrase: "This work is supported by the National Space Biomedical Research Institute through NCC 9-58."

For all funded projects, HRP requests but does not require that scientific manuscripts prepared under HRP or NSBRI support be sent to the office of the HRP Chief Scientist before submission for publication. This is to determine if there may be inadvertent release of identifiable crew information, to identify synergies between projects, and to track program status. It will not be used to otherwise control the content of such manuscripts.

4. Other Considerations

Required Travel

The proposal must include travel costs for the following:

Annual Investigators' Workshop. All NASA and NSBRI Principal Investigators are required to attend the Annual Investigators' Workshop usually scheduled for February of each year in the vicinity of Houston, Texas.

In addition, NSBRI Principal Investigators will be expected to travel to Houston annually to NSBRI Headquarters and demonstration laboratories to exhibit their research.

Optional Travel

Visits to NASA Lyndon B. Johnson Space Center Presentation at a professional society meeting (highly desirable)

G. Submission Dates

Solicitation Announcement Identifier: NRA NNJ15ZSA001N -NSBRI Step-1 Response Period: July 30, 2015 – September 4, 2015 Step-1 Proposals Due: September 4, 2015, 5 PM Eastern Time Step-1 Notification of Proposal Invitation Status: September 24, 2015 Step-2 Response Period: September 24, 2015 – November 23, 2015 Step-2 Proposals Due: November 23, 2015, 5 PM Eastern Time Estimated Step-2 Selection Announcement: April 2016

H. NSBRI Contacts

Additional NSBRI Team and Research Emphases information is available from:

Graham B.I. Scott, Ph.D. Vice President, Chief Scientist & Institute Associate Director National Space Biomedical Research Institute Bioscience Research Collaborative 6500 Main St., Suite 910 Houston, TX 77030 Telephone: 713-798-7227 Fax: 713-798-7413 Email: <u>Graham.Scott@bcm.edu</u>

Additional information on the proposal submission process is available from:

NSPIRES

Telephone: 202-479-9376, Monday through Friday, 8 a.m. to 6 p.m. Eastern Time. Email: <u>nspires-help@nasaprs.com</u>

Frequently Asked Questions: Available through the Proposal Online Help site at <u>http://nspires.nasaprs.com/external/help.do.</u>

Tutorials of NSPIRES: Available at http://nspires.nasaprs.com/tutorials/index.html

I. Summary of Key Information

Selection announcements are expected no earlier than April 2016, and selected awards will begin no earlier than May 2016.

Number of new awards pending	5-7
adequate proposals of merit	
Maximum duration of awards	1 year
First day for submission of Step-1	July 31, 2015
proposals	
Last day for submission of Step-1	September 4, 2015
proposals	
First day for submission of Step-2	September 24, 2015
proposals	
Last day for submission of Step-2	November 23, 2015
proposals	
Page limit for the central Science-	5 pages
Technical section of Step-1 proposal	
Page limit for the central Science-	20 pages
Technical section of Step-2 proposal	
General information and overview of	
this solicitation	Overview posted <u>http://nspires.nasaprs.com</u>
Detailed instructions for the	See NASA Guidebook for Proposers at
preparation and submission of	http://www.hq.nasa.gov/office/procurement/nraguidebook/
proposals	
Submission medium	Electronic proposal submission is required; no hardcopy is
	required. See also HERO Overview and Chapter 3 of the NASA
	Guidebook for Proposers.
Web site for submission of proposal	http://nspires.nasaprs.com/ (help desk available at
via NSPIRES	nspires-help@nasaprs.com or (202) 479-9376)
NSBRI point of contact concerning	Graham B.I. Scott, Ph.D.
this program	